EFFECTIVE DATE NOTE: At 61 FR 4823, Feb. 8, 1996, § 331.25 was removed, effective February 10, 1997.

§ 331.26 Acid neutralizing capacity test.

(a) *pH meter.* Standardize the pH meter at pH 4.0 with the standardizing buffer and check for proper operation at pH 1 with 0.1 N HCl.

(b) *Dosage form testing*—(1) *Liquid sample.* Place an accurately weighed (calculate density) and well mixed amount of product equivalent to the minimum labeled dosage (e.g., 5 ml., etc.) into a 250 ml. beaker. Add sufficient water to obtain a total volume of about 70 ml. and mix on the magnetic stirrer at 300±30 r.p.m. for about one minute. Analyze the sample according to the procedure set forth in § 331.26.

(2) *Chewable and non-chewable tablet sample.* Place an accurately weighed amount of a tablet composite equivalent to the minimum labeled dosage into a 250 ml. beaker. (The composite shall be prepared by determining the average weight of not less than 20 tablets and then comminuting the tablets sufficiently to pass through a number 20 U.S. standard mesh sieve and held by a number 100 U.S. standard mesh sieve. Mix the sieved material to obtain a uniform sample.) If wetting is desired, add not more than 5 ml. of 95 percent ethanol and mix to wet the sample thoroughly (ethanol may effect the acid neutralizing capacity). Add water to a volume of 70 ml. and mix on magnetic stirrer at 300±30 r.p.m. for about one minute. (Capsules should be tested in the same manner using the sieved capsule powder as the sample.) Analyze the sample according to the procedure set forth in § 331.26.

(3) *Effervescent sample.* Place an amount equivalent to the minimum labeled dosage into a 250 ml. beaker. Add 10 ml. water and swirl the beaker gently while allowing the reaction to subside. Add another 10 ml. of water and swirl the beaker gently. Wash down the walls of the beaker with 50 ml. of water and mix on magnetic stirrer at 300±30 r.p.m. for about one minute. Analyze the sample according to the procedure set forth in § 331.26.

(4) *Sample and test procedure for chewing gum with antacid in coating.* Assay six pieces of gum individually in the following manner.

(i) Place one piece of gum in a 250 ml. beaker and add 50 ml. of water.

(ii) Pipette in 30.0 ml. of 1.0 N HCl and stir on magnetic stirrer at 300±30 r.p.m.

(iii) Stir for exactly 10 minutes after addition of acid.

(iv) Stop the stirrer and remove the gum using a long needle or similar utensil.

(v) Rinse the long needle or utensil and the gum with 20 ml. of water into the sample beaker.

(vi) Stir for exactly 5 additional minutes.

(vii) Begin titrating immediately and in a period of time not to exceed 5 minutes titrate the excess 1.0 N HCl with 0.5 N NaOH to stable pH of 3.5.

(viii) Check sample solution 10 to 15 seconds after obtaining pH 3.5 to determine that the pH is stable.

(ix) Average the results of the six individual assays and calculate the total mEq. based on the minimum labeled dosage as follows:

mEq./piece of gum=(30.0 ml.) (normality of HCl)−(ml. of NaOH) (normality of (NaOH). Total mEq. per labeled minimum dose=(number of pieces of gum in minimum dosage)×(mEq./piece of gum).

(c) *Acid neutralizing capacity test procedure* (*except chewing gum*). (1) Pipette 30.0 ml. of 1.0 N HCl into the sample solution while stirring on the magnetic stirrer at 300±30 r.p.m.

(2) Stir for exactly 15 minutes after addition of acid.

(3) Begin titrating immediately and in a period not to exceed an additional 5 minutes titrate the excess 1.0 N HCl with 0.5 N NaOH to stable pH of 3.5.

(4) Check the sample solution 10 to 15 seconds after obtaining pH 3.5 to make sure the pH is stable.

(5) Calculate the number of mEq. of acid neutralized by the sample as follows:

Total mEq.=(30.0 ml.) (normality of HCl)−(ml. of NaOH) (N of NaOH).

Use appropriate factors, i.e., density, average tablet weight, etc., to calculate the total mEq. of acid neutralized per minimum labeled dosage.

[39 FR 19874, June 4, 1974; 39 FR 22140, June 20, 1974]

EFFECTIVE DATE NOTE: At 61 FR 4823, Feb. 8, 1996, § 331.26 was removed, effective February 10, 1997.

§ 331.29 Test modifications.

The formulation or mode of administration of certain products may require modification of this in vitro test. Any proposed modification and the data to support it shall be submitted as a petition under the rules established in § 10.30 of this chapter. All information submitted will be subject to the disclosure rules in part 20 of this chapter.

[47 FR 38480, Aug. 31, 1982]

EFFECTIVE DATE NOTE: At 61 FR 4823, Feb. 8, 1996, § 331.29 was redesignated as § 331.21, and revised, effective February 10, 1997. For the convenience of the reader, the revised text is set forth below.

§ 331.21 Test modifications.

The formulation or mode of administration of certain products may require a modification of the United States Pharmacopeia 23/National Formulary 18 acid neutralizing capacity test. Any proposed modification and the data to support it shall be submitted as a petition under the rules established in § 10.30 of this chapter. All information submitted will be subject to the disclosure rules in part 20 of this chapter.

[61 FR 4823, Feb. 8, 1996]

Subpart D—Labeling

§ 331.30 Labeling of antacid products.

(a) *Statement of identity.* The labeling of the product contains the established name of the drug, if any, and identifies the product as an ''antacid.''

(b) *Indications.* The labeling of the product states, under the heading ''Indications,'' the following: ''For the relief of'' (optional, any or all of the following:) ''heartburn,'' ''sour stomach,'' and/or ''acid indigestion'' (which may be followed by the optional statement:) ''and upset stomach associated with'' (optional, as appropriate) ''this symptom'' or ''these symptoms.'' Other truthful and nonmisleading statements, describing only the indications for use that have been established and listed in this paragraph (b), may also be used, as provided in § 330.1(c)(2) of this chapter, subject to the provisions of section 502 of the act relating to misbranding and the prohibition in section 301(d) of the act against the introduction or delivery for introduction into interstate commerce of unapproved new drugs in violation of section 505(a) of the act.

(c) *Warnings.* The labeling of the product contains the following warnings, under the heading ''Warnings'', which may be combined but not rearranged to eliminate duplicative words or phrases if the resulting warning is clear and understandable:

(1) ''Do not take more than (maximum recommended daily dosage, broken down by age groups if appropriate, expressed in units such as tablets or teaspoonfuls) in a 24–hour period, or use the maximum dosage of this product for more than 2 weeks, except under the advice and supervision of a physician.''

(2) For products which cause constipation in 5 percent or more of persons who take the maximum recommended dosage: ''May cause constipation.''

(3) For products which cause laxation in 5 percent or more of persons who take the maximum recommended dosage: ''May have laxative effect.''

(4) For products containing more than 50 mEq. of magnesium in the recommended daily dosage: ''Do not use this product except under the advice and supervision of a physician if you have kidney disease.''

(5) For products containing more than 5 mEq. sodium in the maximum recommended daily dose: ''Do not use this product except under the advice and supervision of a physician if you are on a sodium restricted diet.''

(6) For products containing more than 25 mEq. potassium in the maximum recommended daily dose: ''Do not use this product except under the advice and supervision of a physician if you have kidney disease.''

(7) For products containing more than 5 gm per day lactose in a maximum daily dosage: ''Do not use this product except under advice and supervision of a physician if you are allergic to milk or milk products.''

(d) *Drug interaction precaution.* The labeling of the product contains the following statements under the heading ''Drug Interaction Precaution'': ''Antacids may interact with certain prescription drugs. If you are presently